THE RISK FACTORS OF BLOOD-BRAIN BARRIER DISRUPTION AFTER ENDOVASCULAR TREATMENT IN PATIENTS WITH CEREBRAL INFARCTION AND ITS RELATIONSHIP WITH EARLY PROGNOSIS

YAN WANG[1,#], CHUNQIAN CAI[2,#], JINQUAN HU[3,*]
[1]Neurotrauma rehabilitation, Characteristic Medical Center of Chinese People's Armed Police Force, Tianjin, 300162, China - [2]Acupuncture and Moxibustion Department, First Teaching Hospital of Tianjin University of Traditional Chinese Medicine, National Clinical Research Center for Chinese Medicine Acupuncture and Moxibustion, Tianjin, 300381, China - [3]Department of Neurology, Taihe Hospital, Hubei University of Medicine, Shiyan, 442000, China
[#]*These authors contributed equally to this work*

ABSTRACT

Introduction: *To explore the risk factors of blood-brain barrier disruption after endovascular treatment in patients with cerebral infarction and its relationship with early prognosis, so as to provide more reference for subsequent prognosis evaluation and the development of more targeted therapeutic schedule.*

Materials and methods: *334 patients with cerebral infarction undergoing endovascular treatment in our hospital from January 2018 to June 2022 were included in this study. They were divided into destruction group (202 cases) and intact group (132 cases) according to the presence or absence of blood-brain barrier disruption. Univariate and multivariate analyses were employed to evaluate the risk factors of blood-brain barrier disruption after endovascular treatment, and analyze the correlation between blood-brain barrier disruption and poor early prognosis.*

Results: *There were statistically significant differences between two groups in concurrent diabetes, randomized blood glucose level, baseline NIHSS score, concurrent cardiogenic embolism, concurrent internal carotid/middle cerebral artery occlusion, poor rate of early prognosis and 90-day follow-up mortality ($P<0.05$). The results of univariate and multivariate analyses of logistic regression model indicated that baseline NIHSS score, concurrent cardiogenic embolism and middle cerebral artery occlusion were independent influence factors of blood-brain barrier disruption after endovascular treatment ($P<0.05$). The incidence of blood-brain barrier disruption in poor prognosis subgroup was significantly higher than that in good prognosis subgroup ($P<0.05$). Multivariate analysis of logistic regression model showed that the occurrence of blood-brain barrier disruption was independently related to poor early prognosis after endovascular treatment ($P<0.05$).*

Conclusion: *The occurrence of blood-brain barrier disruption after endovascular treatment in patients with cerebral infarction is independently related to baseline NIHSS score, concurrent cardiogenic embolism and middle cerebral artery occlusion. At the same time, patients with blood-brain barrier disruption are at a higher risk of poor early prognosis, so more active treatment should be given clinically to maximize the improvement of clinical outcome.*

Keywords: *Cerebral infarction, endovascular treatment, blood-brain barrier disruption, prognosis.*

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Introduction

Previous studies have shown that glucose and oxygen deprivation after cerebral infarction and subsequent reperfusion injury can lead to local energy barrier in brain tissues, form excessive oxidative stress products, and aggravate immune inflammatory injury in brain tissues[1-3]. However, the accumulation of a variety of inflammatory cells at blood-brain barrier site may constantly damage the integrity of barrier, and finally lead to the dysfunction of barrier, significantly increase permeability, and in severe cases, vasogenic cerebral edema or increase of intracranial pressure, which brings adversely effects to treatment and prognosis. Nowadays, there are many reports on blood-brain barrier disruption in patients with cerebral infarction, but no clear conclusion has been drawn as to which

factors are independently related to its occurrence is[4]. Although some reports suggest that blood-brain barrier disruption after cerebral infarction can raise the risk of hemorrhagic transformation, there is insufficient evidence regarding its direct relationship with clinical outcome[5].

In view of the above problems, we aim to provide more reference for subsequent prognosis evaluation and the development of more targeted schedule, by analyzing the risk factors of blood-brain barrier disruption after endovascular treatment in patients with cerebral infarction and their relationship with early prognosis.

Materials and methods

Research objects and grouping

Our study included 334 patients with cerebral infarction who received endovascular treatment in our hospital from January 2018 to June 2022. They were divided into disruption group (202 cases) and intact group (132 cases) according to the presence or absence of blood-brain barrier disruption.

Inclusion criteria:

diagnosed with cerebral infarction clinically;

• Aged 18~80;

• Finished endovascular treatment in our hospital;

• The modified Rankin scale ≤22 points at admission.

Exclusion criteria:

Complicated by cerebral hemorrhage;

• Ischemia scope >1/3 of the blood supply area of brain;

• Hematological diseases;

• With underlying psychiatric or neurological disorders;

• Refused to cooperate in treatment or examination.

Methods

All patients enrolled received endovascular treatment. Specifically: alteplase (0.9 mg/kg) was administered for intravenous thrombolysis, and the duration from onset to treatment was 4.5h; intravascular thrombectomy was performed on patients with persistent arterial occlusion or contraindication to intravenous thrombolysis; the indications and procedures of mechanical thrombectomy were drawn from relevant guidelines of American Heart Association/American Stroke Association, and the duration from onset to treatment was within 6.0h. The data of patients were collected, including gender, age, concurrent chronic disease, random blood glucose level, NIHSS score and treatment. The criteria of blood-brain barrier disruption was drawn from relevant literature, that is, high-density lesions with the leakage of contrast agent can be seen in craniocerebral imaging examination after treatment, the scanning within 24h showed a decrease in the high-density area.

In the meantime, infarct hemorrhagic transformation was excluded[6]. The modified Rankin score and 90-day mortality after surgery were evaluated through follow-up records and the criteria of poor early prognosis was that the modified Rankin score in the 90-day follow-up was 0~1[7].

Statistic analysis

SPSS22.0 software was adopted to process data. The measurement data were compared using a t-test, and ex-pressed as ($\bar{x}\pm s$). The enumeration data were compared using χ^2 test and expressed as %; A logistic regression model was used to evaluate the independent influence fac-tors of blood-brain barrier disruption. $P<0.05$ indicated that the difference was statistically significant.

Results

Comparison of relevant clinical data between disruption group and intact group

There were statistically significant differences between two groups in concurrent diabetes, randomized blood glucose level, baseline NIHSS score, concurrent cardiogenic embolism, concurrent internal carotid/middle cerebral artery occlusion, poor rate of early prognosis and 90-day follow-up mortality ($P<0.05$). There was no significant difference between two groups in relevant clinical data. The data in the disruption group was significantly higher than that in the intact group ($P>0.05$) (Table 1).

Univariate and multivariate analyses of logistic regression model of risk factors of blood-brain barrier disruption

The results of univariate and multivariate analyses of logistic regression model indicated that baseline NIHSS score, concurrent cardiogenic embolism and middle cerebral artery occlusion were independent influence factors of blood-brain barrier disruption after endovascular treatment ($P<0.05$) (Table 2).

Indicator	Disruption Group (n=202)	Intact Group (n=132)	*P*
Age (yrs)	66.89±10.23	67.30±10.65	0.54
Gender (M/F)	123/79	96/36	0.89
Chronic disease type [n, %]			
Hypertension	121 (59.90)	73 (55.30)	0.17
Diabetes	62 (30.69)	23 (17.42)	0.02
Hyperlipidemia	45 (22.28)	25 (18.94)	0.35
Random blood glucose level (mmol/L)	9.74±1.09	8.09±0.85	0.03
Baseline NIHSS score (pts) Concurrent cardiogenic embolism [n, %]	16.94±4.83 123 (60.89)	14.17±3.40 46 (34.85)	0.01 0.00
Internal carotid artery embolism [n, %]	50 (24.75)	27 (20.45)	0.00
Middle cerebral artery embolism [n, %]	64 (32.18)	19 (14.39)	0.00
Endovascular treatment type [n, %]			0.47
Intravenous thrombolysis	80 (39.60)	49 (37.12)	
Mechanical thrombectomy	21 (10.40)	8 (6.06)	
Combined therapy	101 (50.00)	75 (56.82)	
Poor early prognosis [n, %]	76 (37.63)	31 (23.48)	0.02
90-day follow-up mortality [n, %]	21 (10.40)	3 (2.27)	0.01

Table 1: Comparison of relevant clinical data between disruption group and intact group.

Indicator	Univariate			Multivariate		
	OR	95% CI	*P*	*OR*	95% CI	*P*
Cardiogenic embolism	6.70	1.86~13.03	0.00	4.62	1.57~10.33	0.00
Random blood glucose level	1.87	1.03~2.65	0.03	1.23	0.84~1.65	0.27
Baseline NIHSS score	7.54	1.30~19.25	0.00	2.87	1.05~5.75	0.02
Middle cerebral artery occlusion	4.89	1.12~8.67	0.00	3.44	1.16~7.40	0.01

Table 2: Univariate and multivariate analyses of logistic regression model of risk factors of blood-brain barrier disruption.

Correlation analysis between blood-brain barrier disruption and poor early prognosis

117 of the 334 cases had poor early prognosis, accounting for 35.03%. The incidence of blood-brain barrier disruption was 71.03% (76/107) in the poor prognosis subgroup and 55.51% (126/227) in the good prognosis subgroup. The incidence of blood-brain barrier disruption in the poor prognosis subgroup was significantly higher than that in the good prognosis subgroup (P<0.05). Multivariate analysis of logistic regression model showed that the occurrence of blood-brain barrier disruption was independently related to poor early prognosis after endovascular treatment (OR=3.84, 95% CI: 1.26~6.49, P=0.01).

Discussion

Blood-brain barrier disruption is one of the common secondary lesions after stroke. Previous reports have shown that its incidence ranges from 35 to 65%(8-10). 202 of 334 cases included in this study experienced blood-brain barrier disruption, with an incidence of 60.48%. This coincides with the above results. The mechanism of blood-brain barrier disruption after cerebral infarction is complex, and the potential influence factors are still unclear. Some reports demonstrate that the severity of baseline disease and cerebral artery occlusion, etc., may be associated with its occurrence[11, 12]. In our work, the risk factors of blood-brain barrier disruption after endovascular treatment in patients with cerebral infarction were analyzed and the relationship between blood-brain barrier disruption and poor early prognosis was evaluated, through a retrospective analysis of the clinical data of 334 patients with cerebral infarction undergoing endovascular treatment in our hospital from January 2018 to June 2022.

The results of univariate and multivariate analyses in this study showed that baseline NIHSS score, concurrent cardiogenic embolism and middle cerebral artery occlusion were independent influence factors of blood-brain barrier disruption after endovascular treatment (P<0.05). Previous studies have shown that the severity of infarction and the occlusion of feeding arteries in the brain, especially middle cerebral artery, were directly related to the occurrence of blood-brain barrier disruption in patients[13-15]. Our study further supported the above viewpoint. Some scholars have reported that patients with concurrent cardiogenic embolism and cerebral infarction, such as rapid increase of intracranial pressure and secondary hydrocephalus, may undergo mechanical compression in hypothalamus, aggravating ischemia and hypoxia injuries of brain tissues and then inducing the increase of blood-brain barrier permeability and the occurrence of blood-brain barrier disruption[16-19]. The author assumed that this may be the possible mechanism for higher risk of blood-brain barrier disruption in patients with cardiogenic embolism. There is still controversy over the long-term prognosis of patients with blood-brain barrier disruption after cerebral infarction. Some scholars hold that the risk of long-term adverse bleeding events in this group is lower than that in the intact group. But there are also studies indicating that the occurrence of blood-brain barrier disruption

is an independent risk factor for hemorrhagic transformation and malignant cerebral edema in stroke patients[20-23]. According to the results of this study, the incidence of blood-brain barrier disruption in the poor prognosis subgroup was significantly higher than that in the good prognosis subgroup.

At the same time, the occurrence of blood-brain barrier disruption was independently related to poor early prognosis after endovascular treatment, implying that clinicians should classify patients with cerebral infarction and blood-brain barrier disruption as a high-risk group for poor prognosis and give more active and effective intervention, so as to minimize neurological deficit and reduce the risk of death and disability. There are also some shortcomings in this study: it belongs to single-center retrospective reports, and the effect of selection bias cannot be ruled out. The conclusion remains to be confirmed by larger-scale multi-center prospective studies; our study takes the exudation of contrast media as the criterion for judging blood-brain barrier disruption. Although it is widely used and easy to operate, it is still necessary to explore more reliable and accurate ways to determine blood-brain barrier disruption[18].

To sum up, the occurrence of blood-brain barrier disruption after endovascular treatment in patients with cerebral infarction is independently related to baseline NIHSS score, concurrent cardiogenic embolism and middle cerebral artery occlusion. At the same time, patients with blood-brain barrier disruption are at a higher risk of poor early prognosis, so more active treatment should be given clinically to maximize the improvement of clinical out-come.

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Corresponding Author:
Jinquan Hu
The Hospital, Hubei University of Medicine, 32 Renmin Road, Shiyan City, Hubei Province
Email: ccq56287806@163.com
(China)